

1/13

Figure 1: Nucleic Acid coding sequence human histamine H4

ATGCCAGATACTAATAGCACAAATCAATTTATCACTAAGCACTCGTGTTACTTTAGCATTT
TTTATGTCCTTAGTAGCTTTTGCTATAATGCTAGGAAATGCTTTGGTCATTTTAGCTTTTG
TGGTGGACAAAAACCTTAGACATCGAAGTAGTTATTTTTTCTTAACCTGGCCATCTCTG
ACTTCTTTGTGGGTGTGATCTCCATTCTTTGTACATCCCTCACACGCTGTTCTGAATGGG
ATTTTGGAAAGGAAATCTGTGTATTTTGGCTCACTACTGACTATCTGTTATGTACAGCAT
CTGTATATAACATTGTCCTCATCAGCTATGATCGATACCTGTCAGTCTCAAATGCTGTGT
CTTATAGAACTCAACATACTGGGGTCTTGAAGATTGTTACTCTGATGGTGGCCGTTTGG
GTGCTGGCCTTCTTAGTGAATGGGCCAATGATTCTAGTTTCAGAGTCTTGGAAGGATGA
AGGTAGTGAATGTGAACCTGGATTTTTTTCGGAATGGTACATCCTTGCCATCACATCATT
CTTGGAATTCGTGATCCCAGTCATCTTAGTCGCTTATTTCAACATGAATATTTATTGGAG
CCTGTGGAAGCGTGATCATCTCAGTAGGTGCCAAAGCCATCCTGGACTGACTGCTGTCT
CTTCCAACATCTGTGGACACTCATTCAGAGGTAGACTATCTTCAAGGAGATCTCTTTCTG
CATCGACAGAAGTTCCTGCATCCTTTCATTTCAGAGAGACAGAGGAGAAAGAGTAGTCTC
ATGTTTTCTCAAGAACCAAGATGAATAGCAATACAATTGCTTCCAAAATGGGTTCCTT
CTCCCAATCAGATTCTGTAGCTCTTCACCAAAGGGAACATGTTGAACTGCTTAGAGCCA
GGAGATTAGCCAAGTCACTGGCCATTCTCTTAGGGGTTTTTGCTGTTTGCTGGGCTCCAT
ATTCTCTGTTTACAATTGTCCTTTCATTTTATTCCTCAGCAACAGGTCCTAAATCAGTTTG
GTATAGAATTGCATTTTGGCTTCAGTGGTTCAATTCCTTTGTCAATCCTCTTTGTATCCA
TTGTGTCACAAGCGCTTTCAAAAGGCTTTCTTGAAAATATTTTGTATAAAAAAGCAACC
TCTACCATCACAACACAGTCGGTCAGTATCTTCTTAA

Figure 2: Amino acid sequence human histamine H4 receptor

Met Pro Asp Thr Asn Ser Thr Ile Asn Leu Ser Leu Ser Thr Arg Val Thr Leu
Ala Phe Phe Met Ser Leu Val Ala Phe Ala Ile Met Leu Gly Asn Ala Leu Val
Ile Leu Ala Phe Val Val Asp Lys Asn Leu Arg His Arg Ser Ser Tyr Phe Phe
Leu Asn Leu Ala Ile Ser Asp Phe Phe Val Gly Val Ile Ser Ile Pro Leu Tyr
Ile Pro His Thr Leu Phe Glu Trp Asp Phe Gly Lys Glu Ile Cys Val Phe Trp
Leu Thr Thr Asp Tyr Leu Leu Cys Thr Ala Ser Val Tyr Asn Ile Val Leu Ile
Ser Tyr Asp Arg Tyr Leu Ser Val Ser Asn Ala Val Ser Tyr Arg ThrGln His
Thr Gly Val Leu Lys Ile Val Thr Leu Met Val Ala Val Trp Val Leu Ala Phe
Leu Val Asn Gly Pro Met Ile Leu Val Ser Glu Ser Trp Lys Asp Glu Gly Ser
Glu Cys Glu Pro Gly Phe Phe Ser Glu Trp Tyr Ile Leu Ala Ile Thr Ser Phe
Leu Glu Phe Val Ile Pro Val Ile Leu Val Ala Tyr Phe Asn Met Asn Ile Tyr
Trp Ser Leu Trp Lys Arg Asp His Leu Ser Arg Cys Gln Ser His Pro Gly Leu
Thr Ala Val Ser Ser Asn Ile Cys Gly His Ser Phe Arg Gly Arg Leu Ser Ser
Arg Arg Ser Leu Ser Ala Ser Thr Glu Val Pro Ala Ser Phe His Ser Glu Arg
Gln Arg Arg Lys Ser Ser Leu Met Phe Ser Ser Arg Thr Lys Met Asn Ser Asn
Thr Ile Ala Ser Lys Met Gly Ser Phe Ser Gln Ser Asp Ser Val Ala Leu His
Gln Arg Glu His Val Glu Leu Leu Arg Ala Arg Arg Leu Ala Lys Ser Leu Ala
Ile Leu Leu Gly Val Phe Ala Val Cys Trp Ala Pro Tyr Ser Leu Phe Thr Ile
Val Leu Ser Phe Tyr Ser Ser Ala Thr Gly Pro Lys Ser Val Trp Tyr Arg Ile
Ala Phe Trp Leu Gln Trp Phe Asn Ser Phe Val Asn Pro Leu Leu Tyr Pro Leu
Cys His Lys Arg Phe Gln Lys Ala Phe Leu Lys Ile Phe Cys Ile Lys Lys Gln
Pro Leu Pro Ser Gln His Ser Arg Ser Val Ser Ser

Figure 3: Tissue Distribution of human histamine H4 receptor

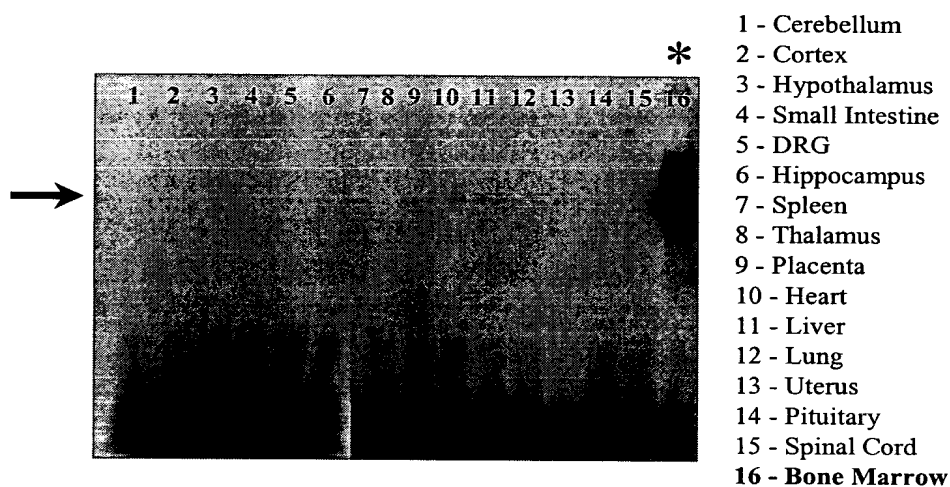


Figure 4: Binding of [³H]-histamine to pH4R expressing COS7 cells.

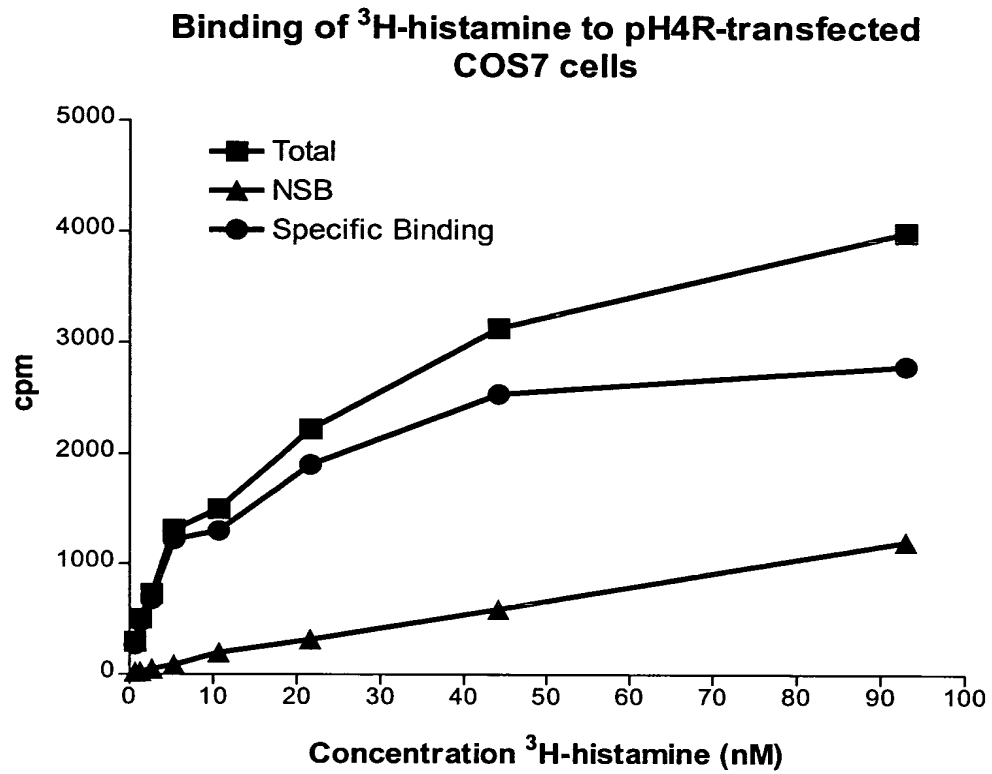


FIGURE 5A

Mouse H4 DNA coding region (SEQ.ID.NO.:5)

ATGTCGGAGTCTAACAGTACTGGCATCTTGCCACCAGCTGCTCAGGTCCCCTTGGCATTTTTAATGT
CTTCATTTGCCTTTGCTATAATGGTAGGCAATGCTGTGGTCATCTTAGCCTTTGTGGTGGACAGAAA
CCTTAGACATCGAAGTAATTATTTTTTCTTAATTTGGCTATTTCTGACTTCCTCGTGGGTTTGATT
TCCATTCTCTGTACATCCCTCACGTGTTGTTAACTGGAATTTGGAAGTGGAACTGTCATGTTTT
GGCTCATTACTGACTATCTTTTGTGCACCGCATCTGTCTACAATATTGTCCTCATTAGCTACGATCG
ATACCAGTCAGTTTCAAATGCTGTGTCTTATAGGGCTCAACACACTGGCATCATGAAGATTGTTGCT
CAAATGGTGGCTGTTTGGATACTGGCTTCTTGGTAAATGGCCCGATGATTCTGGCTTCAGATTCTT
GGAAGAACAGCACGAACACAAAGGACTGTGAGCCTGGCTTTGTTACAGAGTGGTACATCCTCACCAT
TACAATGCTCTTGGAATTCCTGCTTCCTGTCATCTCTGTGGCTTATTTCAATGTACAGATTTACTGG
AGCCTGTGGAAGCGTAGGGCTCTCAGTAGGTGCCCTAGCCATGCTGGATTCTCCACTACCTCTTCCA
GTGCTTCAGGACACTTACACAGAGCTGGGGTGGCTTGCAGGACAAGTAATCCTGGATTGAAGGAATC
AGCTGCATCTCGTCACTCAGAAAGTCCTCGAAGAAAGAGCAGCATCCTGGTGTCTTAAGGACTCAC
ATGAACAGCAGTATCACTGCCTTCAAAGTGGGTTCCTTCTGGCGATCGGAAAGTGCAGCGCTTCGCC
AAAGGGAGTACGCAGAGCTTCTCAGAGGCAGGAAGCTAGCCAGGTCACTGGCCATCCTTCTGAGCGC
TTTTGCCATTTGCTGGGCTCCATACTGTCTGTTTACAATTGTCTTTCACTTACCCAGAACGGAA
CGCCCCAAATCGGTGTGGTACAGCATTGCCTTCTGGCTGCAATGGTTCAATTCGTTTGTAAATCCCT
TTCTGTACCCTTTGTGTACAGGCGTTTCCAGAAGGCTTTCTGGAAGATACTTTGTGTGACAAAGCA
ACCAGCGCTGTACAGAACCAGTCAGTATCTTCTTGA

FIGURE 5B

Rat H4 DNA coding region (SEQ.ID.NO.:6)

ATGTCGGAGTCTAACGGCACTGACGTCTTGCCACTGACTGCTCAAGTCCCCTTGGCATTTTTAAATGT
CCCTGCTTGCTTTTGCTATAACGATAGGCAATGCTGTGGTCATTTTAGCCTTTGTAGCAGACAGAAA
CCTTAGACATCGAAGTAATTATTTTTTTCTTAATTTGGCTATTTCTGACTTCTTCGTGGGTGTCATC
TCCATTCTCTGTACATCCCTCACACGCTGTTAACTGGAATTTTGAAGTGGAATCTGCATGTTTT
GGCTCATTACTGACTATCTTTTGTGCACAGCATCCGTCTACAGTATTGTCCCTATTAGCTACGATCG
ATACCAGTCAGTTTCAAACGCTGTGCGTTATAGAGCACAGCACACTGGCATCCTGAAAAATTGTTGCT
CAAATGGTGGCTGTTTGGATACTGGCTTTCTTGGTCAATGGCCCAATGATTCTGGCTTCGGATTCTT
GGAAGAACAGCACCAACACAGAGGAGTGCGAGCCTGGCTTTGTTACTGAGTGGTACATCCTCGCCAT
TACAGCATTCTTGAATTCCCTGCTCCCTGTCTCCTTGGTGGTCTATTTTCAGTGTACAGATTTACTGG
AGCCTGTGGAAGCGTGGGAGTCTCAGTAGGTGCCCTAGCCACGCTGGATTTCATCGCTACCTCTTCCA
GGGGCACTGGACACTCACGCAGAACTGGGTTGGCTTGTAGGACAAGTCTTCCTGGATTAAAGGAACC
AGCCGCATCCCTTCATTCAGAAAGTCCACGAGGAAAGAGCAGTCTCCTGGTGTCCCTAAGGACTCAC
ATGAGCGGTAGTATCATCGCCTTCAAAGTGGGTTCCCTTCTGCCGATCAGAAAGCCCAGTGCTTCACC
AGAGAGAGCACGTGGAGCTTCTCAGAGGCAGGAAGCTAGCCAGGTCGCTAGCTGTCCCTCCTGAGTGC
TTTTGCCATTTGCTGGGCTCCGTATTGCCTGTTTCAAAATTGTTCTTTCAACTTATCGCAGAGGGGAG
CGCCCCAAATCGATTTGGTACAGCATAGCCTTTTGGCTACAGTGGTTCAATTCACCTATTAATCCCT
TTCTATACCCTTTGTGCCACAGACGTTTCCAGAAGGCTTTCTGGAAGATACTCTGTGTGACAAAGCA
ACCAGCACCTTCACAGACCCAGTCAGTATCTTCTTGA

FIGURE 5C

Guinea Pig H4 DNA coding sequence (SEQ.ID.NO.:7)

ATGTTGGCAAATAACAGTACAATCGCCTTAACATCAATTAATAATTTCTTTGACATTTTAA
ATGTCCTTTACTAGCTATTGCTATAATGTTAGGCAATGTCGTGGTCATTTTAGCTTTTATTG
TGGACAGAAATCTTAGACATCGAAGTAATTACTTTTTCTTAACCTGGCCATTGCAGACT
TCTTTGTGGGTGCAATTGCAATTCCTCTGTACATACCTTCCTCGCTGACTTACTGGACTT
CTGGAAGCAAGCTTGTGTATTTTGGCTCATTACTGACTATCTTTTATGtACAGCATCTGT
GTATAATATTGTCCTCATCAGCTACGATCGCTACCAGTCAGTCTCAAATGCCGTGTGGTA
TAGAGCTCAGCACTCTGGCACCTGGAAAATTGCTACTCAGATGGTGGCTGTTTGGATAT
TCTCCTTCATGACAAAATGGGCCGATGATTCTGATTTTCAAGCTCTTGGCAGAATAGCACT
ACAGAATGTGAACCTGGATTTTTAAAAAAGTGGTACTTTGCTCTCCCTACATCATTATTG
GAATTCCTGATCCCCATCTTGTTAGTTGCTTATTTTCAAGCGCCCATATTTACTGGAGCCTG
TGGAAGCGAGAGAAACTGAGCAGGTGCCTCAGCCACCCTGTAATCCCCTCTGACTCTTC
CAGCAGTGACCACGGACACTCCTGCAGACAGGACCCCGATTCAAGGGCGACTCTGCCA
GCACGGAAAGAAACAACCTGCCTCTCTTGGTTTCAAGTACAGGAGAAAGAGCAGTC
TCTTGTTTTCCATAAGAGCCTACAAGAACAGCAATGTGATCGCTTCCAAAATGGGCTTC
CTCTCCCCTCAGATTCCTGGCTCTTCAGCAAAGGGAACATATCGAACTTTTTCAGAGC
CAGGAAATTAGCCAAGTCACTGGCCATACTCTTAGCAGCTTTTGGCATTGCTGGGCTCC
ATATTCAGTACTACAGTTATCTACTCATTTTTTCTGAAAGGAACTTGACTAAATCAAC
CTGGTACCATACTGCCTTTTGGCTCCAGTGGTTCAATTCCTTTGTTAATCCCTTTTGTAT
CCATTGTGTCAAAACGTTTTTCAGAAAGGCTTTCCTGAAAATACTTCCTGTGAGAAGGCA
ATCCACGCCACCACACAACCGCTCAATATCCACTTGA

8/13

FIGURE 6A

Mouse histamine H4 receptor protein sequence (SEQ.IN.NO.:8)

MSESNSTGILPPAAQVPLAFLMSSFAFAMVGNNAVILAFVVDNRNLRHRSNYFFLNLAISDFL
VGLISIPLYIPHVLFNWNFGSGICMFWLITDYLLCTASVYNIVLISYDRYQSVSNAVSYRAQH
TGIMKIVAQMVAVWILAFVLNGPMILASDSWKNSTNTKDCEPGFVTEWYILTITMLLEFLLP
VISVAYFNVQIYWSLWKRRALSRCPSHAGFSTTSSSASGHLHRAGVACRTSNPGLKESAASR
HSESPRRKSSILVSLRTHMNSSITAFKVGSFWRSESAALRQREYAELLRGRKLARSLAILLSA
FAICWAPYCLFTIVLSTYPRTERPKSVWYSIAFWLQWFNSFVNPFLYPLCHRRFQKAFWKIL
CVTKQPALSQNQSVSS

FIGURE 6B

Rat histamine H4 receptor protein sequence (SEQ.ID.NO.:9)

MSESNGTDVLPLTAQVPLAFLMSLLAFITIGNAVVILAFVADRNLRRHSNYFFLNLAISDFF
VGVISIPLYIPHTLFNWNFGSGICMFWLITDYLLCTASVYSIVLISYDRYQSVSNVRYRAQH
TGILKIVAQMVAVWILAFVNGPMILASDSWKNSTNTEECEPGFVTEWYILAITAFLEFLLPV
SLVVYFSVQIYWSLWKRGSLSRCPHAGFIATSSRGTGHSRRTGLACRTSLPGLKEPAASLH
SESPRGKSSLLVSLRTHMSGSHAFKVGSFCRSESPVLHQREHVELLRGRKLARSLAVLLSAF
AICWAPYCLFTIVLSTYRRGERPKSIWYSIAFWLQWFNSLINPFLYPLCHRRFQKAFWKILCV
TKQPAPSQTQSVSS

10/13

FIGURE 6C

Guinea Pig histamine H4 receptor protein sequence (389 amino acids)
(SEQ.ID.NO.:10)

MLANNSTIALTSIKISLTFLMSLLAIAIMLGNVVVILAFIVDRNLRHRSNYFFLNLAIAIDFFVG
AIAIPLYIPSSLTYWTSGKQACVFWLITDYLLCTASVYNIVLISYDRYQSVSNVWYRAQHS
GTWKIATQMVA VWIFSMTNGPMILISDSWQNSTTECEPGFLKKWYFALPTSLLLEFLIPILLV
AYFSAHIYWSLWKREKLSRCLSHPVLPSSSSSDHGHSCRQDPDSRATLPARKETTASLGSD
KSRRKSSLLFSIRAYKNSNVIASKMGFLSHSDSLALQQREHIELFRARKLAKSLAILLAFAIC
WAPYSLTTVIYSFFPERNLTKSTWYHTAFWLQWFNSFVNPFLYPLCHKRFQKAFLKILPVRR
QSTPPHNRSIST

Figure 7A
Nucleotide Sequence Comparison of Human (SEQ ID NO:1), Guinea Pig (SEQ ID NO:7), Mouse (SEQ ID NO:5), and Rat H4 (SEQ ID NO:6)

[illegible]

Figure 7B

Human: CCATATTCCTCTGTTCACAAAATGTCCTTTCAATTTTATTCTCTCAGCAACAGGTCCCTAAATCAGTTTGGTATAGAATTGCAATTTGGCTTCAGTGGTTCAATTCCTTTGTCAATCCTCTTTTG 1071
Guinea Pig: CCATATTCACGTGACTACAGTTATCTACTCAATTTTCTCTGAAAGGAACCTGACTAAATCAACCTGGTACCATACCTGCTTTTGGCTCCAGTGGTTCAATTCCTTTGTAAATCCCTTTTG 1071
Mouse: CCATACCTGCTGTTTCAACAATGTCCTTTCAACTTACCCAGAACGGAACGCCCCAAATCGGTGTTGGTACAGCATTTGCTTCTGGCTGCAATGGTTCAATTCGTTGTTAAATCCCTTTCTG 1077
Rat: CCGTATGCTGTTTCAACAATGTTCTTTCAACTTATCGCAGAGGGAGCGCCCCAAATCGAATTTGGTACAGCATAGCCTTTTGGCTACAGTGGTTCAATTCACCTTATTAAATCCCTTTCTA 1077

Human: TATCCATTGTGTCACAAGGGCTTTCAAAAGGCTTTCTTGAAATAATTTTGTATAAAAAGCAACCTCTACCATCAACAACAGTCGGTCAGTATCTTCTTAA 1173
Guinea Pig: TATCCATTGTGTCACAAGGCTTTTCAGAAAGGCTTTCTTGAAATAACTTCTCTGTGAGAGGCAATCCACGCCACCA --- CACAACCGCTCAATATCCACTTGA 1170
Mouse: TACCCCTTTGTGTACAGGCTTTCCAGAAAGGCTTTCTGGAAGATACTTTGTGTGACAAAGCAACCAAGCGCTGTCA --- CAGAACCAGTCAGTATCTTCTTGA 1176
Rat: TACCCCTTTGTGCCACAGAGGTTTCCAGAAAGGCTTTCTGGAAGATACTCTGTGTGTGACAAAGCAACCAAGCACCTTCA --- CAGACCCAGTCAGTATCTTCTTGA 1176

Figure 8

Amino Acid sequence Comparison of Human (SEQ ID NO:2), Guinea Pig (SEQ ID NO:10), Mouse (SEQ ID NO:8) and Rat H4 (SEQ ID NO:9)

Human:	MPDTNSTINLSLSTRVTLAFEMSLVAFAIMLGNALVILAFVVDKLNLRHRSYFFFLNLAISDFFVGVISIPLYIPHTLFEWDFGKEICVFWLTDTYLLCTA	100
Guinea Pig:	MLANNSTIALT-SIKISLTFILMSLLAIAIMLGNVVVILAFIVDRNLNRHRSNYFFFLNLAIADEFFVGAIAIPLYIPSSLTWTSGKQACVFWLTDTYLLCTA	99
Mouse:	MSESNSTGILPPAAQVPLAFLMSSFAFAIMVGNVAVILAFVVDNRNLNRHRSNYFFFLNLAISDFLVGLISIPLYIPHVLENNWFGSGICMFWLTDTYLLCTA	100
Rat:	MSESNSTGTDVPLPLTAQVPLAFLMSSLLAFATITIGNAVVILAFVADNRNLNRHRSNYFFFLNLAISDFFVGVISIPLYIPHTLFEWDFGKEICVFWLTDTYLLCTA	100
Consensus:	M . . N . T . L . : : : : L . E . MSL : A : AIM : GN : : VILAF : : D : NLRHRS : YFFLNLA : DF : VG . I : IPLYIP . : L W . G : C : FWL . TDYLLCTA	
	TM1	
	TM2	
	TM3	
Human:	SVYNIVLISYDRYLSVSNVAVSYRTQHTGVLKIVTLMVAVWVILAFVNGPMILVSESWKDEG-S-ECEPGFFSEWYIIAITSFLEFVIPVILVAYFNMNIY	198
Guinea Pig:	SVYNIVLISYDRYQSVSNVAVYRAQHSQGTWKIATQMVAWVIFSEFTNGPMILISDSWQNST-T-ECEPGFLKKWYFALPTSLLEFLIPILVAYFSAHIY	197
Mouse:	SVYNIVLISYDRYQSVSNVAVYRAQHTGIMKIVAQMVAVWILAFVNGPMILASDSWKNSTNKDCEPGFVTEWYITITMLLEFLLPVISVAYFNVQIY	200
Rat:	SVYSIVLISYDRYQSVSNVAVYRAQHTGILKIVAQMVAVWILAFVNGPMILASDSWKNSTNTECEPGFVTEWYIIAITSFLEFLPVSLVVFVFSVQIY	200
Consensus:	SVYNIVLISYDRY SVSNVAV YR:QH:G. KI. . . MVAVW: : : F. . NGPMIL: S:SW: . . . : CEPGF: . . WY: . . . T. : LEF: : P: . . VAYF: . . IY	
	TM4	
	TM5	
Human:	WSLWKRDHLSRCQSHPG-L-TAVSSNICGHSFRGLSSRRSLASASTEVPAFHSERQRRKSSLMFSSRTKMNSNTIASKMGFSQSQSDSVALHQREHVELLR	297
Guinea Pig:	WSLWKREKLSRCLSHPVLPDSSSDHGHSCRPDPDSRATLPARKETASLGSDKRRKSSILFSIRAYKNSNVIAASKMGFLSHSDSLAQOREHIELER	297
Mouse:	WSLWKRRALSRCPSHAGF-STTSSASAGHLHRAGVACRTSNPGLKESAAASHSESPRRKSSILVSLRTHMNSSITAFKVGFWSESAALRQREYAEELLR	299
Rat:	WSLWKRGSLSRCPSHAGF-IATSSRGTHSRRTGLACRTSLPGLKEPAASLHSESPRGKSSLLVSLRTHMSSIIAFKVGSCFRCSESPVLHQIEHVELLR	299
Consensus:	WSLWKR: . LSRC SH. : : . SS. GH. R . : R : : : . . E. . AS: S: : R. KSSL: S R: A. K: G : : S: S: L: Q E: : EL: R	
Human:	ARLAKSLAILLGVFVAVCWAPYSLFTIVLSFYSSATGPKSVWYRIAFWLQWFNSFVNPLLYPLCHKRFQKAFKILFCIKKQPLPSQHSRSVSS	390
Guinea Pig:	ARKLAKSLAILLAFAICWAPYSLFTVIYSFFPERNLTKSTWHTAFWLQWFNSFVNPLYPCHKRFQKAFKILPVRRQSTPP-HNRSIST	389
Mouse:	GRKLARSLAILLSAFAICWAPYCLFTIVLSTYPTERPKSVWYSIAFWLQWFNSFVNPLYPCHRRRFQKAFKILCVTKQPALSQ-NQSVSS	391
Rat:	GRKLARSLAVLLSAFAICWAPYCLFTIVLSTYRRGERPKSIWYSIAFWLQWFNSLINFPLYPLCHRRRFQKAFKILCVTKQAPPSQ-TQSVSS	391
Consensus:	. R: LA: SLA: LL: . FA: CWAPY: L T: : S : : . . . KS. WY: . . AFWLQWFNS: . NP: LYPLCH: RFQKAF. KI: : : Q: . : : RS: S:	
	TM6	
	TM7	